A COMPARATIVE STUDY OF SURGICAL OUTCOME OF TRABECULECTOMY WITH OLOGEN IMPLANT VERSUS MITOMYCIN C IN A TERTIARY CARE CENTRE OF WEST BENGAL

Sandip Samaddar[1], Somnath Das[2], Sumit Gupta[3]

[1]Assistant Professor, Department of Ophthalmology, Regional Institute of Ophthalmology, Medical College, Kolkata.
[2]Associate Professor, Department of Ophthalmology, Regional Institute of Ophthalmology, Medical College, Kolkata.
[3]Postgraduate Trainee, Department of Ophthalmology, Regional Institute of Ophthalmology, Medical College, Kolkata.

ABSTRACT

BACKGROUND

Glaucoma affects more than 67 million persons worldwide of whom about 10% or million are estimated to be blind. In India, 12.8% of blindness are reported to occur due to glaucoma. Trabeculectomy is the standard surgical procedure for the reduction of Intraocular Pressure (IOP) in glaucoma patients. But, introduction of adjunctive antimetabolites like Mitomycin C (MMC) and Ologen, a biodegradable, porous, porcine, collagen implant significantly decrease the postoperative subconjunctival scarring with formation of an ideal bleb leading to improved long-term success of trabeculectomy.

The aim of the study is to compare the outcomes of trabeculectomy with or without Ologen implant and adjunctive antimetabolites in patients requiring glaucoma surgery for uncontrolled intraocular pressure.

MATERIALS AND METHODS

This prospective randomised comparative study was conducted in the glaucoma clinic at the Regional Institute of Ophthalmology (RIO), Medical College and Hospital, Kolkata, during a period of 12 months (January 2015 - January 2016). 60 glaucomatous eyes (either POAG or PACG) of patients who are attending glaucoma clinic of RIO during the study period and were fit for filtration surgery were selected by simple random selection.

RESULTS

MMC and Ologen implant have better success rate over simple trabeculectomy in terms of IOP control. There was no statistically significant difference between the three groups regarding age. The absolute success rate at 6th month postoperatively were 60% in group 1 and 80% in group 2 and group 3 showing no significant difference between group 2 and group 3. But, the success rate was significantly lower in trabeculectomy group than that of other two groups.

CONCLUSION

Ologen implant in trabeculectomy could be a new, safe and effective alternative treatment to MMC with similar success rate on 6 months follow up. This implant may for instance be preferred when antimetabolite related risks need to be avoided.

KEYWORDS

Glaucoma, Adjunctive, Intraocular Pressure, Trabeculectomy, Adjunctive Antimetabolites, Ologen.

HOW TO CITE THIS ARTICLE: Samaddar S, Das S, Gupta S. A comparative study of surgical outcome of trabeculectomy with Ologen implant versus mitomycin C in a tertiary care centre of West Bengal. J. Evid. Based Med. Healthc. 2017; 4(85), 5001-5004. DOI: 10.18410/jebmh/2017/997

BACKGROUND

Glaucoma affects more than 67 million persons worldwide, of whom, about 10% or million are estimated to be blind[1] and it is the second only to cataract as the most common cause of blindness.[2,3] The estimated prevalence of glaucoma in India is 11.9 million.[4] In India, 12.8% of blindness is reported to occur due to glaucoma.[4]

Trabeculectomy, introduced by Cairns in 1968, remains the standard surgical procedure for the reduction of Intraocular Pressure (IOP) in patients with medically-controlled glaucoma worldwide.[5,6] The reported success rate for primary trabeculectomies varies from 75%-100% in POAG.[7] The aim of trabeculectomy is to lower IOP in order to slow the progression of glaucomatous optic neuropathy and visual loss.[8,9]

The outcome of this surgery depends upon the formation of a functioning shunt for aqueous drainage from the eye leading to development of a filtration bleb. Scarring of structures at the trabeculectomy site including conjunctiva, episclera, scleral flap and ostium may lead to poor formation of bleb, and hence, T-shunt function resulting in suboptimal control of IOP. So, inhibition of scar formation during the process of wound healing should promote greater success.[10,11]

With the introduction of adjunctive antimetabolites, like Mitomycin C (MMC), which significantly decrease the

Financial or Other, Competing Interest: None.
Submission 03-10-2017, Peer Review 09-10-2017,
Acceptance 19-10-2017, Published 21-10-2017.
Corresponding Author:
Dr. Somnath Das,
Bagati, Professor Para, Post Office and Police Station,
Mogra, Hooghly District - 712148, West Bengal.
E-mail: somnathdas1969@gmail.com
DOI: 10.18410/jebmh/2017/997

postoperative subconjunctival scarring have improved the long-term success of trabeculectomy.[12,13,14,15]

Ologen, a biodegradable, porous, porcine, collagen implant was designed aiming to improve the long-term success of trabeculectomy. It acts by decreasing the subconjunctival scarring and is associated with less bleb-related complications.[16] At the end of the trabeculectomy, the collagen implant is placed subconjunctivally over the scleral flap. The implant helps to facilitate the formation of loose connective tissue matrix by acting as a scaffold for growth of fibroblast into the pores of the implant and thus aims to help tissue remodeling and decrease the scar formation. The implant not only acts as a reservoir, but also helps to mechanically separate the conjunctiva and episcleral surface and prevent adhesions between them.[16,17]

The purpose of the study is to compare the outcomes of trabeculectomy with or without Ologen implant and adjunctive antimetabolites in patients requiring glaucoma surgery for uncontrolled intraocular pressure.

Aims and Objective- To compare the outcomes of trabeculectomy with or without Ologen implant and adjunctive antimetabolites in patients requiring glaucoma surgery for uncontrolled IOP. Our specific objective was to compare the postoperative IOP level between the groups.

MATERIALS AND METHODS

This prospective randomised comparative study was conducted in the glaucoma clinic at the Regional Institute of Ophthalmology (RIO), Medical College and Hospital, Kolkata, during a period of 12 months (January 2015 - January 2016). 60 glaucomatous eyes (either POAG or PACG) of patients who are attending glaucoma clinic of RIO during the study period and were fit for filtration surgery were selected by simple random selection.

All the acute and chronic Primary Angle-Closure Glaucoma (PACG) patients and Primary Open-Angle Glaucoma (POAG) patients with progression of visual field loss and/or uncontrolled IOP levels with medications were included in our study.

Patients aged less than 18 years, cases of neovascular glaucoma, normal tension glaucoma, acute or chronic disease that could confound the outcomes of the study (e.g., immunodeficiency, connective tissue disease, diabetes, hypertension, history of ocular trauma, previous ocular surgery except cataract surgery) and patients who had known allergic reaction to collagen were excluded from our study. Randomisation done to allot the patients into 3 groups- 1. Group 1 included 20 eyes that will undergo trabeculectomy; 2. Group 2 included 20 eyes that will undergo trabeculectomy with adjunctive antimetabolites (MMC); and 3. Group 3 included 20 eyes that will undergo trabeculectomy with collagen (Ologen) implant (6 mm diameter and 2 mm height).

Snellen's visual acuity chart, streak retinoscope, trial lenses and box, Goldmann applanation tonometer, Goldmann two mirror gonioscope, pachymetry, direct and indirect ophthalmoscope, slit-lamp biomicroscopy with +90D, Humphrey Field Analyser II, Anterior Segment Optical Coherence Tomography (AS-OCT) were used for this study. Before going through ocular examination, a detailed history was taken. Personal interview was conducted to determine exposure to risk factors of glaucoma like family history of glaucoma, ocular trauma, past eye surgery and past treatment for glaucoma. History was taken and general checkup was done to rule out diabetes and hypertension. All surgeries were performed by a single experienced competent surgeon. In group 3 patients, the implant (6 mm diameter and 2 mm height) was positioned on top of the scleral flap before conjunctival closure.

Postoperatively, patients of all the 3 groups were reviewed on day 1, 2 weeks, 1 month, 3 months and at 6 months. IOP were measured on 1 month, 3 months and 6 months by Goldmann applanation tonometer.

Absolute success was defined as TOP, on 6^{th} month postoperatively, lower than 18 mm of Hg without any additional topical medication. Qualified success was defined as IOP equal to or more than 18 mm of Hg without any additional topical medication, on 6^{th} month postoperatively.

Using the formula for intervention study, the sample size for each intervention group can be calculated as $n=z\times z\times 2\times S\times S/L\times L$. Where Z=2, S=0.5 mm of Hg and L=0.1%. Putting the values in this formula, the sample size has been calculated 20 in each intervention group.

Regarding concealment allocation, there were 60 sealed envelopes of similar shape, size and colour. Inside each envelope, type of operation was written. Whenever a patient was selected to enter the study, an envelope was opened. Blinding was not done in our study, because surgeon himself was part of the study.

As IOP is a continuous variable, we have used ANOVA with post HOC Tukey's test to test for difference of IOP in between the treatment groups. P <5% was considered to be significant. Statistical analysis was performed with the help of Epi Info (TM) 3.5.3.

At all the 3 observations, IOP was significantly associated with the type of intervention.

Regarding IOP control, there is nothing to choose between (trabeculectomy with MMC) or (trabeculectomy with Ologen) as both groups achieved similar IOP at 1, 3 and 6 months.

Statistical analysis was performed with help of Epi Info (TM) 3.5.3. EPI Info is a trademark of the Centers for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to prepare different frequency tables and to calculate the means with corresponding standard errors. Chi-square test was applied as the measures of associations.

RESULTS

Group	Age Group(yrs.)				Total	Mean ± SD
	40-49	50-59	60-69	70-79		
Trabeculectomy	7	4	4	5	20	56.75 ± 11.49
Row%	35	20	20	25	100	
Col%	30.4	28.6	30.8	50	33.3	
Trabeculectomy + MMC	9	4	4	3	20	55.30 ± 11.85
Row%	45	20	20	15	100	
Col%	39.1	28.6	30.8	30	33.3	
Trabeculectomy + Ologen	7	6	5	2	20	56.15 ± 9.48
Row%	35	30	25	10	100	
Col%	30.4	42.9	38.5	20	33.3	
Total	23	14	13	10	60	
Row%	38.3	23.3	21.7	16.7	100	
Col%	100	100	100	100	100	

Table 1. Age Distribution of Subjects

Group	Type of Glaucoma		Total
	PACG	POAG	
Trabeculectomy	11	9	20
Row%	55	45	100
Col%	30.6	37.5	33.3
Trabeculectomy + MMC	14	6	20
Row%	70	30	100
Col%	38.9	25	33.3
Trabeculectomy + Ologen	11	9	20
Row%	55	45	100
Col%	30.6	37.5	33.3
Total	**36**	**24**	**60**
Row%	**60**	**40**	**100**
Col%	**100**	**100**	**100**

Table 2. Distribution of the Type of Glaucoma among Subjects

Group	Type of Surgery		Total
	Phaco + Trab	Trab	
Trabeculectomy	18	2	20
Row%	90	10	100
Col%	38.3	15.4	33.3
Trabeculectomy + MMC	15	5	20
Row%	75	25	100
Col%	31.9	38.5	33.3
Trabeculectomy + Ologen	14	6	20
Row%	70	30	100
Col%	29.8	46.2	33.3
Total	**47**	**13**	**60**
Row%	**78.3**	**21.7**	**100**
Col%	**100**	**100**	**100**

Table 3. Distribution of Types of Surgery Performed

Postoperative Time	Trabeculectomy (Group 1) (n=20)	Trabeculectomy + MMC (Group 2) (n=20)	Trabeculectomy + Ologen (Group 3) (n=20)	'p' value by ANOVA Test
Month 1	17.50 ± 0.57	15.10 ± 0.06	13.80 ± 0.03	0.001
Month 3	17.50 ± 0.50	14.00 ± 0.72	14.10 ± 0.68	0.0003
Month 6	16.90 ± 0.27	14.40 ± 0.59	13.60 ± 0.53	0.0001

Table 4. Mean (±SD) of IOP on Postoperative Months of the Subjects

DISCUSSION

Aimed to improve the long-term surgical success of trabeculectomy, but with less attendant complications of MMC, Ologen, a bioengineered porcine collagen has been developed.[16,17]

In our study, the mean age in group 1 (trabeculectomy) was 56.75 ± 11.49 years; among them, 10 (50%) were males and 10 (50%) were females. The mean age in group 2 (trabeculectomy with MMC) was 55.30 ± 11.85 years; among them, 11 patients (55%) were males and 9 patients (45%) were females. The mean age in group 3 (trabeculectomy with Ologen) were 56.15 ± 9.48 years; among them, 13 patients (65%) were males and 7 patients (35%) were females. Chi-square test showed that there was no significant association between gender (p=0.62), age (p=0.87) and the three study group. Thus, the groups were gender and age matched. The male-female ratio was 1.3:1. 11 eyes in group 1 (55%) had PACG; 9 eyes (45%) had POAG. In group 2, 14 eyes (70%) had PACG and 6 eyes (30%) had POAG. Finally, in group 3, 11 eyes (55%) had PACG; 9 eyes (45%) had POAG. Chi-square test showed that there was no significant association between type of glaucoma and three study groups (p=0.53). 18 eyes (90%) in group 1 underwent trabeculectomy with phacoemulsification, while 2 eyes (10%) underwent only trabeculectomy. In group 2, 15 eyes (75%) underwent combined trabeculectomy with phacoemulsification and 5 eyes (25%) underwent only trabeculectomy. In group 3, 14 eyes (70%) underwent combined surgery and 6 eyes (30%) underwent trabeculectomy. No significant association between type of surgery and three study groups (p=0.27). One month postoperatively, the mean IOP was 17.50 ± 0.57 mm of Hg in group 1, 15.10 ± 0.06 mm of Hg in group 2 and 13.80 ± 0.03 mm of Hg in group 3. As per the Critical Difference (CD), the mean IOP of Group 1 was significantly highest of all the three groups (p<0.01). But, there was no statistically significant difference between mean IOP of Group 2 and Group 3 (p >0.05). At 3 months postoperatively, the mean IOP in group 1 was 17.50 ± 0.50 mm of Hg; in group 2 was 14.00 ± 0.72 mm of Hg; and in group 3 was

14.10 ± 0.68 mm of Hg. As per the CD, the mean IOP of Group 1 was significantly highest of all the three groups ($p<0.05$). But, there was no statistically significant difference between mean IOP of Group 2 and Group 3 ($p >0.05$). At 6 months postoperatively, the mean IOP was 16.90 ± 0.27 mm of Hg, 14.40 ± 0.59 mm of Hg and 13.60 ± 0.53 mm of Hg in group 1, group 2 and group 3, respectively. There was no statistically significant difference between mean IOP of Group 2 and Group 3 ($p >0.05$), while the mean IOP in group 1 was significantly higher of all three groups ($p <0.05$). This result is similar to that of prospective randomised study by Cillino et al[18] in 2011 comparing the safety and efficacy of Ologen as adjuvant compared with low-dosage MMC in 40 patients with two years followup. Papaconstantinou et al[19] in their pilot study have compared trabeculectomy with and without Ologen implant. With a 6 month follow-up and a sample size of 20 eyes in each group, they reported similar success rate, but this is in contrast to the result of Rosenteter et al[20] who compared 10 eyes each in trabeculectomy with MMC and Ologen groups and reported significantly higher complete success rate (IOP <18 mmHg and at least 20% reduction of preoperative IOP) at the end of 12 months in trabeculectomy with MMC group (100% with MMC vs. 50% with Ologen, P - 0.01). However, all cases in their cases were POAG and they had only 10 cases in each group.

CONCLUSION

In conclusion, our study suggests that the Ologen implant in trabeculectomy could be a new, safe and effective alternative treatment to MMC with similar success rate on 6 months follow up. This implant may for instance be preferred when antimetabolite related risks need to be avoided. The postoperative complications were also similar in the three groups. The limitations of this study were high cost of Ologen, the small number of patients, a particular region and that the study sample was not population based. Due to our relatively small sample size, which limits the statistical comparison between the groups, further larger randomised trials with long-term follow up regimen are required to investigate the long-term efficacy and safety of this new device. Also, the high cost of Ologen limits its affordability among a major group of population.

REFERENCES

[1] Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90(3):262-267.

[2] Cook C, Foster P. Epidemiology of glaucoma: what's new? Can J Ophthalmol 2012;47(3):223-226.

[3] Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol 1996;80(5):389-393.

[4] Jacob A, Thomas R, Koshi SP, et al. Prevalence of primary glaucoma in an urban south Indian population. Indian J Ophthalmol 1998;46(2):81-86.

[5] Cairns JE. Trabeculectomy. Preliminary report of a new method. Am J Ophthalmol 1968;66(4):673-679.

[6] Watson PG, Barnett F. Effectiveness of trabeculectomy in glaucoma. Am J Ophthalmol 1975;79(5):831-845.

[7] Agarwal HC, Sharma TK, Silhota R, et al. Cumulative effect of risk factors on short term surgical success of mitomycin augmented trabeculectomy. J Postgrad Med 2002;48(2):92-96.

[8] Vogel R, Crick RP, Newson RB, et al. Association between intraocular pressure and loss of visual field in chronic simple glaucoma. Br J Ophthalmol 1990;74(1):3-6.

[9] O'Brien C, S'chwartz B, Takamoto T, et al. Intraocular pressure and the rate of visual field loss in chronic open angle glaucoma. Am J Ophthalmol 1991;111(4):491-500.

[10] Skuta GL, Parrish RK. Wound healing in glaucoma filtering surgery. Surv Ophlhalmol 1987;32(3):149-I70.

[11] Mietz H, Arnold G, Kirchhof B, et al. Histopathology of episcleral fibrosis after trabeculectomy with and without mitomycin C. Graefes Arch Clin Exp Ophthalmol 1996;234(6):364-368.

[12] Bindlish R, Condon GP, Schlosser JD, et al. Efficacy and safety of mitomycin-C in primary trabeculectomy: five-year follow-up. Ophthalmology 2002;109(7):1336-1341; discussion 1341-2.

[13] Lama PJ, Fechtner RD. Antifibrotics and wound healing in glaucoma surgery. Surv Ophthalmol 2003;48(3):314-346.

[14] Beckers HJ, Kinders KC, Webers CA. Five-year results of trabeculectomy with mitomycin C. Graefes Arch Clin Exp Ophthalmol 2003;241(2):106-110.

[15] Katz GJ, Higginbotham EJ, Lichter PR, et al. Mitomycin C versus 5-fluorouracil in high-risk glaucoma filtering surgery. Extended follow-up. Ophthalmology 1995;102(9):1263-1269.

[16] Chen HS, Ritch R, Krupin T, et al. Control of filtering bleb structure through tissue bioengineering: an animal model. Invest Ophthalmol Vis Sci 2006;47(12):5310-5314.

[17] Hsu WC, Ritch R, Krupin T, et al. Tissue bioengineering for surgical bleb defects: an animal study. Graefes Arch Clin Exp Ophthalmol 2008;246(5):709-717.

[18] Cillino S, Di Pace F, Cillino G, et al. Biodegradable collagen matrix implant vs mitomycin-C as an adjuvant in trabeculectomy: a 24-month, randomized clinical trial. Eye (Lond) 2011;25(12):1598-1606.

[19] Papaconstantinou D, Georgalas I, Karmiris E, et al. Trabeculectomy with Ologen versus trabeculectomy for the treatment of glaucoma: a pilot study. Acta Ophthalmol 2010;88(1):80-85.

[20] Rosentreter A, Schild AM, Jordan JF, et al. A prospective randomised trial of trabeculectomy using mitomycin C vs. an Ologen implant in open angle glaucoma. Eye (Lend) 2010;24(9):1449-1457.